International Journal of Infectious Diseases 17 (2013) e289–e292

Contents lists available at SciVerse ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Review

Human brucellosis in the People's Republic of China during 2005–2010

Zhijun Zhong [a,b,1], Shuang Yu [a,1], Xichun Wang [c,1], Shicun Dong [d], Jie Xu [b], Yufei Wang [b], Zeliang Chen [b], Zhihua Ren [a], Guangneng Peng [a,*]

[a] Key Laboratory of Animal Disease and Human Health of Sichuan Province, College of Veterinary Medicine, Sichuan Agricultural University, Ya'an 625014, P. R. China
[b] Department of Infectious Disease Control, Beijing Institute of Disease Control and Prevention, Beijing, P.R. China
[c] College of Animal Science and Technology, Anhui Agricultural University, Hefei, P.R. China
[d] Qinghai Center for Disease Control and Prevention, Xining, P.R. China

ARTICLE INFO

Article history:
Received 18 May 2012
Received in revised form 22 November 2012
Accepted 21 December 2012

Corresponding Editor: Eskild Petersen, Skejby, Denmark

Keywords:
Human brucellosis
Epidemiology
People's Republic of China

SUMMARY

Brucellosis is a worldwide re-emerging zoonotic disease. It remains a serious public health problem in many developing countries including China. This review summarizes the epidemiological characteristics, morbidity, and endemic distributions of human brucellosis in the People's Republic of China for the period 2005–2010. From 2005 to 2010, the incidence of human brucellosis rose substantially in China, especially in the provinces of Inner Mongolia, Shanxi3, Heilongjiang, Hebei, Jilin, and Shanxi1. Meanwhile human brucellosis increased gradually in some southern provinces, such as Henan, Guangdong, and Fujian. Due to the rapid expansion of human brucellosis in China, surveillance and prevention of this disease has been greatly challenged.

1. Introduction

Brucellosis, especially that caused by *Brucella melitensis*, is an old disease and yet is the most common zoonotic disease worldwide, with an annual occurrence of more than 500 000 cases and prevalence rates exceeding 10 cases per 100 000 population in some countries.[1,2] Humans are infected by this pathogen mainly through contact with infected animals or by consuming unpasteurized and unboiled milk or fresh cheese.[1] On entry into the human, the pathogens multiply inside phagocytic cells and eventually cause clinical symptoms, such as undulant fever, abortion, orchitis, spondylitis, arthritis, endocarditis, encephalitis, and asthenia. Brucellosis is listed as a Class II reportable disease by the Centers for Disease Control and Prevention (CDC) of the People's Republic of China and as a Class II key disease by the Disease Prevention and Control of Livestock and Poultry in China.[3] More importantly it is classified by the CDC as a class B bioterrorist agent, as *Brucella spp* can easily be aerosolized, and thus could be used to develop a biological weapon. Of note, the geographical distribution of brucellosis changes dynamically, with new foci emerging or re-emerging worldwide. Thus, as a re-emerging infectious disease, human brucellosis requires robust and enhanced surveillance in many areas.[4]

In China, human brucellosis was first reported in 1905.[5] Serial investigations of the epidemiological characteristics of brucellosis have been carried out since 1950. The incidence of brucellosis was quite severe in animals and humans before the 1980s and later declined. From 1990 to 2001, the incidence of animal brucellosis remained unchanged, but the incidence of human brucellosis increased greatly.[3] In 2008, 21 surveillance points for animal and human brucellosis were established in 19 provinces in order to tightly monitor/prevent the onset of disease.[6] Several vaccines have been developed for disease prevention and control, such as *Brucella suis* S2, *Brucella abortus* S19, and *B. melitensis* M5. Remarkably China is one of the few countries where the vaccines have been used to prevent human brucellosis (*B. abortus* 104 M).[3] However, the epidemiology of the human brucellosis situation became more severe during 2005–2010.

In this paper, the epidemiological characteristics, morbidity, and endemic distributions of human brucellosis were analyzed for 31 provinces with high incidence rates of brucellosis, for the period 2005–2010, in accordance with the criteria of the CDC of the People's Republic of China.

2. Materials and methods

2.1. Data source

The data in this study were extracted from medical cases occurring during 2005–2010. The number of human brucellosis

* Corresponding author. Tel.: +86 0835 2885302; fax: +86 0835 2885302.
E-mail address: pgn.sicau@163.com (G. Peng).
[1] These authors contributed equally to this work.

1201-9712/$36.00 – see front matter
http://dx.doi.org/10.1016/j.ijid.2012.12.030

cases was obtained from the Ministry of Health of the People's Republic of China and the CDC of the People's Republic of China. Any suspected or confirmed case of brucellosis in China must be reported to the Chinese CDC through the National Notifiable Disease Surveillance System. The report of human cases must be accompanied by clinical signs and confirmed by serologic test or isolation of the organism, in accordance with the case definition of the World Health Organization.[7,8]

2.2. Education campaigns, surveillance points, and intervention pilot

In China, education campaigns to reduce the risk and consequences of human brucellosis disease have been designed and launched by the CDC of the People's Republic of China and executed by local provincial governments and CDCs. The National Brucellosis Surveillance Points for Human and Animal Brucellosis and the National Brucellosis Intervention Pilot County are the two major programs.[6,9] The two programs include seven aspects: (1) strengthening the supervising responsibility of local governments and departments; (2) improving the preventive treatment in human brucellosis and the professional skills of the experts; (3) monitoring of human brucellosis epidemics and improving the reporting system of outbreaks to the CDC; (4) executing the prevention of animal brucellosis; (5) epidemic situations must be investigated by the joint forces of the Ministry of Health and the Ministry of Agriculture; (6) provincial CDCs supervise the control and prevention of human and animal brucellosis; (7) promoting education campaigns for health awareness and increasing the knowledge of the population with regard to the prevention of human and animal brucellosis.

2.3. Data analysis

The statistics in this study were analyzed using SPSS software (version 17.0). A linear regression model was used to assess the incidence rate of the time trend in each province during 2005–2010,[10] year (X) as the independent variable and Y as the dependent variable. Y is the incidence rate of the natural logarithm (as $Y = \ln(r)$). p-Values of <0.05 were considered statistically significant.

3. Results

3.1. Overview of human brucellosis incidence in China

As shown in Figure 1, the annual reported cases of human brucellosis showed an upward trend from 2005 to 2009, and a slight decline in 2010. In 2005, a total of 18 416 cases were reported. Thereafter a steep increase in human brucellosis cases was reported during 2008–2009. The peak disease incidence occurred in 2009, with 35 816 cases reported, almost double the cases from 2005. In 2010 there was a slight decline (33 772 cases), but the number of cases remained higher than the annual reports for 2005–2007. At the same time, the annual incidence rate of the disease varied from 1.41 to 2.7 per 100 000 population during the study period (Figure 1). The rate in 2005 was 1.41 cases per 100 000 population, but showed an upward trend in the following years. In 2009 and 2010, the rate rose to 2.7 and 2.56/100 000, respectively. Compared to the rate in 2005, the rate had tripled in 2009 and 2010, showing a dramatic change over the 6 years.

3.2. Analysis of human brucellosis in 31 provinces of China

As shown in Table 1, 18 provinces reported new cases of human brucellosis in 2005, but the epidemic regions expanded to 30 provinces of P.R. China (except for Hong Kong, Macao, Taiwan, and Jiangxi) over the 6 years.

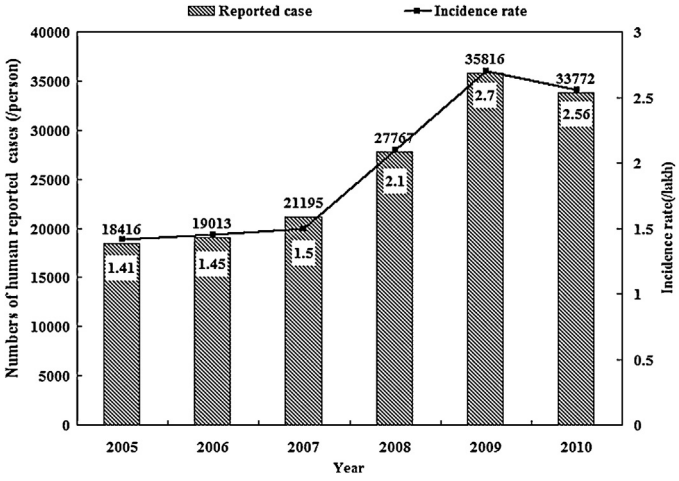

Figure 1. Reported cases and annual incidence (n/100 000 population) of human brucellosis in the People's Republic of China during 2005–2010.

During 2005–2010, a total of 155 979 new cases were reported in China. Inner Mongolia, Shanxi3, Heilongjiang, Hebei, Jilin, and Shanxi1 were the top six provinces with the most cases. Inner Mongolia had 69 092 reported cases, or 50% of all the reported cases in China. As shown in Table 1, Inner Mongolia had the most reported cases in 2009 and 2010 (16 551 and 16 224 cases, respectively). The annual incidence rate varied from 33.17 to 68.33 per 100 000 population during the study period, which is much higher than in the other provinces ($p < 0.01$). In Shanxi3 Province, the number of reported cases increased sharply from 2005 to 2008. The annual incidence rate rose from 6.92 to 14.17 per 100 000 population during 2005–2008, and declined slightly during 2009–2010 (13.91 and 10.88 per 100 000 population). In contrast to Shanxi3 Province, the reported number of cases in Heilongjiang Province showed a decrease from 2005 to 2007. However, the reported cases increased 1.93 times in 2010 when compared to 2007. In Hebei Province, the number of reported cases kept an upward trend during 2005–2009, rising from 1181 to 3218. Compared to other provinces, the number of reported cases in Jilin Province increased greatly in recent years. The number of cases increased markedly from 2007 to 2009, with 12 times the annual incidence: an increase from 1.92 per 100 000 population in 2005 to 12.60 per 100 000 population in 2009 ($p < 0.01$). In Shanxi1 Province, there was an increase in reported cases and then a decline (483 cases in 2005 and 1034 cases in 2008, then 911 and 525 cases in 2009 and 2010, respectively).

Moreover, reported cases and annual incidence rates in Henan, Xinjiang, Ningxia, Gansu, Guangdong, and Fujian provinces all showed an increasing trend during the study period ($p < 0.05$) (Table 1). Especially in Henan and Ningxia provinces, more cases were reported in 2010 (791 and 207 cases, respectively). In Henan, the annual incidence rate showed a significant upward trend in the period 2005–2010 ($p < 0.01$). The annual incidence in Ningxia rose from 0.44 to 3.27 per 100 000 population in the period of 2005–2010 ($p < 0.05$). Remarkably in 2010, the very first case of brucellosis was reported in Hainan Province since the founding of new China in 1949.

The regional distribution of the lowest and highest annual reported cases were applied to analyze the geographic distribution of human brucellosis in China (Figure 2, A and B). From the regional distribution map, it is clearly demonstrated that the areas with heavy brucellosis epidemics are mainly located in the northern provinces of China, particularly those in the northeast and

Table 1
Reported cases and annual incidence rate (/100 000 population) of human brucellosis in 31 provinces in China during 2005–2010

Province	2005	2006	2007	2008	2009	2010	*p*-Value
Inner Mongolia	8663 (36.31)	7951 (33.17)	8598 (35.75)	11 105 (46.01)	16 551 (68.33)	16 224 (65.63)	0.14
Shanxi3	2320 (6.92)	3452 (10.23)	4447 (13.11)	4834 (14.17)	4768 (13.91)	3888 (10.88)	0.169
Heilongjiang	3943 (10.33)	2949 (7.71)	2523 (6.60)	3670 (9.59)	4724 (12.35)	4861 (12.68)	0.227
Hebei	1181 (1.73)	2334 (3.38)	2567 (3.70)	3173 (4.54)	3218 (4.57)	2503 (3.48)	0.129
Jilin	521 (1.92)	599 (2.20)	985 (3.61)	2139 (7.82)	3452 (12.60)	2905 (10.58)	0.003
Shanxi1	483 (1.30)	636 (1.70)	793 (2.12)	1034 (2.75)	911 (2.42)	525 (1.41)	0.559
Liaoning	604 (1.43)	439 (1.03)	374 (0.87)	484 (1.12)	509 (1.18)	606 (1.39)	0.786
Henan	141 (0.15)	194 (0.21)	337 (0.36)	593 (0.63)	703 (0.74)	791 (0.84)	0.001
Xinjiang	297 (1.48)	263 (1.29)	326 (1.56)	395 (1.86)	441 (2.04)	797 (3.65)	0.021
Shandong	163 (0.18)	108 (0.12)	142 (0.15)	135 (0.14)	156 (0.16)	222 (0.23)	0.262
Ningxia	26 (0.44)	7 (0.12)	32 (0.52)	94 (1.52)	157 (2.51)	207 (3.27)	0.027
Zhejiang	25 (0.05)	24 (0.05)	13 (0.03)	34 (0.07)	38 (0.07)	31 (0.06)	0.436
Gansu	5 (0.02)	6 (0.02)	8 (0.03)	6 (0.02)	84 (0.32)	46 (0.18)	0.045
Guangdong	3 (0.00)	14 (0.02)	15 (0.02)	18 (0.02)	27 (0.03)	35 (0.03)	0.019
Tianjin	11 (0.11)	4 (0.04)	8 (0.07)	14 (0.12)	24 (0.20)	56 (0.43)	0.058
Beijing	8 (0.05)	9 (0.06)	4 (0.02)	12 (0.07)	17 (0.10)	29 (0.15)	0.129
Tibet	21 (0.76)	8 (0.28)	2 (0.07)	2 (0.07)	1 (0.03)	0 (0.00)	0.010
Yunnan	0 (0.00)	1 (0.00)	1 (0.00)	10 (0.02)	12 (0.03)	8 (0.02)	0.082
Jiangsu	0 (0.00)	5 (0.01)	3 (0.00)	5 (0.01)	6 (0.01)	5 (0.01)	0.542
Anhui	0 (0.00)	2 (0.00)	1 (0.00)	2 (0.00)	7 (0.01)	4 (0.01)	0.175
Fujian	0 (0.00)	1 (0.00)	2 (0.01)	4 (0.01)	3 (0.01)	5 (0.01)	0.039
Sichuan	0 (0.00)	6 (0.01)	0 (0.00)	1 (0.00)	1 (0.00)	2 (0.00)	0.355
Qinghai	1 (0.02)	0 (0.00)	6 (0.11)	0 (0.00)	0 (0.00)	3 (0.05)	0.668
Shanghai	0 (0.00)	0 (0.00)	5 (0.03)	2 (0.01)	0 (0.00)	0 (0.00)	-
Guangxi	0 (0.00)	0 (0.00)	2 (0.00)	0 (0.00)	1 (0.00)	3 (0.01)	0.874
Guizhou	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	3 (0.01)	1 (0.00)	-
Chongqing	0 (0.00)	1 (0.00)	0 (0.00)	0 (0.00)	2 (0.01)	0 (0.00)	-
Hubei	0 (0.00)	0 (0.00)	1 (0.00)	0 (0.00)	0 (0.00)	5 (0.01)	-
Hunan	0 (0.00)	0 (0.00)	0 (0.00)	1 (0.00)	0 (0.00)	9 (0.01)	-
Hainan	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (0.00)	-
Jiangxi	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	-

northwest, which have developed areas of animal husbandry with frequent livestock product transactions.[3] Figure 2 shows that the epidemics in the old regions were still not effectively controlled and that they expanded into southern regions of China. During 2005–2010, the incidence of brucellosis showed increasing tendencies in Henan, Guangdong, and Fujian provinces ($p < 0.05$). These data indicate that human brucellosis is likely to expand from the epidemic regions to the non-epidemic provinces.

4. Discussion

At present, 15 of the total 19 biotypes of Brucella have been isolated in China, including *B. melitensis* (biotypes 1, 2, and 3), *B. abortus* (biotypes 1–7 and 9), *B. suis* (biotypes 1 and 3), *B. ovis*, and *B. canis*.[3,11] From 2005 to 2006, of the more than 100 strains isolated, *B. melitensis* was the predominant strain.[12] In 2009, 75 strains were isolated in 15 provinces, of which 68 strains were *B. melitensis* biotype 3, accounting for 90.7%, indicating that the major epidemic strain in China was *B. melitensis* biotype 3.[12] Recent studies have implied that strains isolated from southern China had the same MLVA-16 genotype (multilocus variable number tandem repeat analysis 16 loci panel) as those from northern and eastern China, indicating that brucellosis in the south may have originated from the importation of animals from elsewhere in China.[13]

Before the 1980s, the epidemic regions of human brucellosis were distributed in Inner Mongolia, Xinjiang, Tibet, Qinghai, Ningxia, and other scattered epidemic provinces.[3] In our study we found that in the period 2005–2010, the human brucellosis epidemic remained in the northeastern provinces (i.e., Inner Mongolia and northern China) where animal husbandry has developed. The rising incidence rate could have a potential correlation to the trans-boundary transfer of animal brucellosis in the region of Inner Mongolia from the neighboring hyperendemic Mongolia, which has been described as the country with the second highest incidence worldwide.[2] The increase in animal feeding, lack of immunization and animal quarantine, and frequent trading are the leading risk factors for the high incidence rate. Moreover, a complete monitoring system would be able to report the incidence data in an unbiased manner. Therefore, it is of importance for the local and provincial CDC to control/prevent human brucellosis in the most epidemic cities.

Human brucellosis cases have mainly appeared in particular key cities in endemic areas of China; Hulunbeir and Xilinguole in Inner Mongolia, Datong in Shanxi3, Qiqihaer in Heilongjiang, Zhangjiakou in Hebei, Songyuan in Jilin, and Yulin in Shanxi1 showed the highest human brucellosis incidence.[8,14,15] Among those cities, the number of reported cases in Hulunbeir reached a record high of 2798 cases in 2005.[8,14] In Songyuan, the number of newly reported cases has increased continuously in recent years. In 2008, 1019 new cases were reported, which is twice the reported number in 2005.[15]

In China, a national brucellosis eradication program has been implemented since the 1990s. There are 21 human brucellosis surveillance points and 10 animal surveillance points in China, which monitor brucellosis outbreaks in time.[6] Meanwhile, a project named the National Brucellosis Intervention Pilot County was also set up in 2005 to survey and prevent animal and human brucellosis.[9] Human brucellosis in most provinces was effectively controlled due to better surveillance and prevention rules. Although many measures based on the control programs for brucellosis have been set up (including slaughtering infected animals), the brucellosis-positive rate in animals has increased significantly. In 2008, 3.5 million cattle (dairy cattle 3.24 million) were examined by serological tests and the positive rate was 0.64% (0.58% dairy cattle); 10 999 positive cattle were slaughtered (including dairy cattle 10 362). Sheep were also tested; the positive rate was 0.84% for 4.74 million sheep, and 11 329 positive sheep were killed.[12] In 2009, of a total of 41 736 sheep, 626 were found to be seropositive (positive rate = 1.49%); a total of 62 843 cattle were

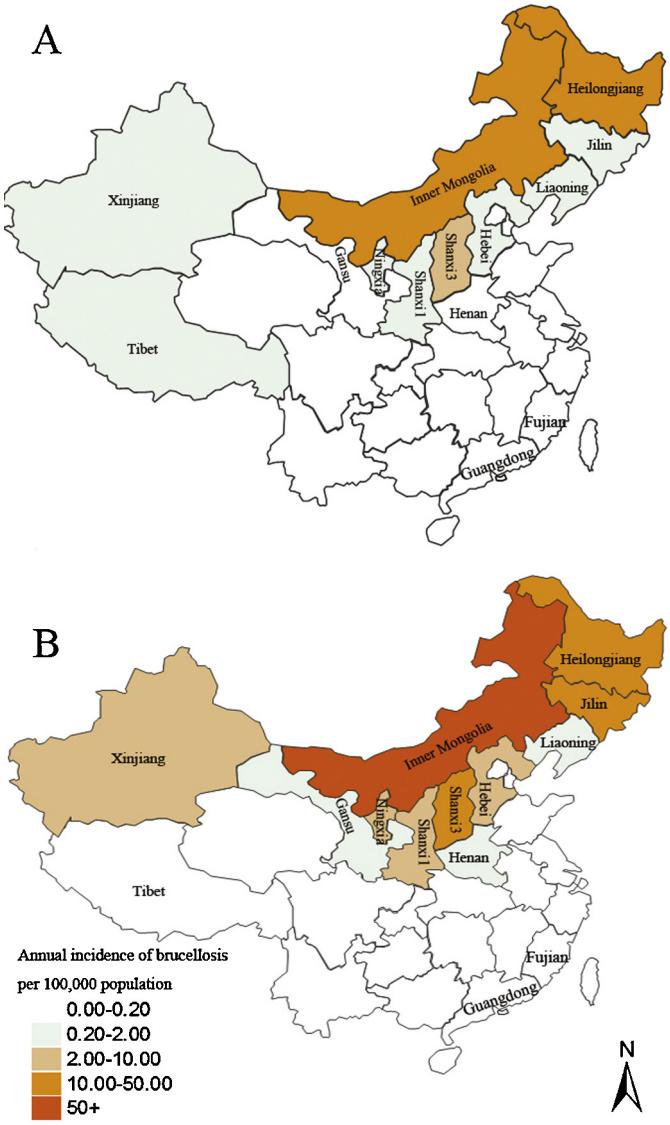

Figure 2. Geographic distribution by annual incidence of human brucellosis in (A) 2005 and (B) 2009, People's Republic of China.

examined and 852 were found to be seropositive (positive rate = 1.36%).[12] The high brucellosis-positive rate in animals could be one of the factors that has led to the increase in human brucellosis cases in recent years.

Our study is limited by several unavoidable factors. First, since the data derived from 31 provinces were aggregated data, the quality of the data cannot be controlled. Second, the data reported directly by the disease reporting system of the provinces is only part of the actual incidence of human brucellosis. Third, the misdiagnosis rate is high in low-incidence areas and the under-reporting phenomenon is serious. Nevertheless, the data analyzed in this study are still able to reflect the current trend in the incidence of human brucellosis in China. Our investigation is potentially helpful to establish strategies for the prevention and surveillance of human brucellosis in China and in other countries.

In conclusion, our data show that human brucellosis occurred mainly around the border with Inner Mongolia (except Xinjiang Province), and brucellosis outbreak points also increased significantly during 2005–2010. At the same time, endemic regions gradually spread to some southern provinces, including Henan, Guangdong, and Fujian. More non-epidemic provinces have become epidemic, which implies that the epidemic regions of brucellosis had diversification. It is necessary to develop better strategies for brucellosis prevention and control in the near future.

Acknowledgements

We thank Dr Zhen Liu for the English language revision. This work was supported by the National Basic Research Program of China (Grant No. 2009CB522602), National Natural Science Foundation of China (31000548, 31000041, 81071320), and Program for Changjiang Scholars and Innovative Research Team in University (IRT0848).

Conflict of interest: The authors have no conflicts of interest to disclose.

References

1. Pappas G, Akritidis N, Bosilkovski M, Tsianos E. Brucellosis. *N Engl J Med* 2005;**352**:2325–36.
2. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV. The new global map of human brucellosis. *Lancet Infect Dis* 2006;**6**:91–9.
3. Deqiu S, Donglou X, Jiming Y. Epidemiology and control of brucellosis in China. *Vet Microbiol* 2002;**90**:165–82.
4. Memish ZA, Balkhy HH. Brucellosis and international travel. *J Travel Med* 2004;**11**:49–55.
5. Boone HW. Malta fever in China. *China Medicine Mission* 1905;**19**:167–73.
6. Jiang H, Mao LL, Zhao HY, Li LY, Piao DR, Tian GZ, et al. Reemergence and genetic comparison of *Brucella canis* in China, using a multiple-locus variable-number tandem-repeat assay. *Vet Microbiol* 2012;**154**:419–21.
7. Ministry of Health of the People's Republic of China. Brucellosis diagnostic criteria and treatment principles. Beijing: China People's Health Publishing House; 2008. p. 71–3.
8. Zhang WY, Guo WD, Sun SH, Jiang JF, Sun HL, Li SL, et al. Human brucellosis, Inner Mongolia, China. *Emerg Infect Dis* 2010;**16**:2001–3.
9. Liu FQ, Wang DL, Wang JQ, Li TF, Zhao YL, Sen L. National brucellosis intervention pilot county survey on the economic losses. *Chinese Journal of Control of Endemic Diseases* 2008;**23**:424–5.
10. Jung KW, Park S, Won YJ, Kong HJ, Lee JY, Seo HG, et al. Prediction of cancer incidence and mortality in Korea, 2012. *Cancer Res Treat* 2012;**44**:25–31.
11. Jiao XA, Huang JJ. Prevalence and control strategies of bacterial zoonoses in pets. *Chinese Journal of Comparative Medicine* 2010;**20**:59–64.
12. Man TF, Wang DL, Cu BY, Wang Y, Ding F, Li TF, et al. Analysis on surveillance data of brucellosis in China, 2009. *Disease Surveillance* 2010;**25**:944–6.
13. Jiang H, Fan M, Chen J, Mi J, Yu R, Zhao H, et al. MLVA genotyping of Chinese human *Brucella melitensis* biovar 1, 2 and 3 isolates. *BMC Microbiol* 2011;**11**:256.
14. Gao QY. Epidemiological survey of brucellosis in Songyuan City in 2008. *China Tropical Medicine* 2010;**12**:1495.
15. Mi JC, Zhang QH, Wei RP, Song LT, Zheng Z. The epidemiological characteristics of human brucellosis in Inner Mongolia. *Chinese Journal of Control of Endemic Diseases* 2010;**25**:34–6.